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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,422	11/21/2000	Jamel Chelly	P06780US0/BAS	1213

881 7590 09/08/2003

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EXAMINER
SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,422	CHELLY ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *2,4-7 and 10-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,8,9 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. The amendment filed 20 February 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The deletion of specific nucleotide sequences ahs broadened the aspect of just what the nucleotide sequence to encompass virtually any primer. While he specification does identify the primers by a name, a specific nucleotide sequence is no longer associated with the name.

Applicant is required to cancel the new matter in the reply to this Office Action.

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The disclosure is objected to because of the following informalities: The specification has been found to contain conflicting characterizations of what SEQ ID NO:26 represents. At page 3, penultimate paragraph, said SEQ ID NO:26 is described as being a "cDNA fragment," while at page 14, lines 26-27, it is an "aminoacid [sic] sequence, and at page 15, lines 2-3, it is defined as being a "polypeptide."

Appropriate correction is required.

Response to Amendment

4. In the amendment of July 8, 2002, claim 1 was amended such that it is directed towards SEQ ID NO: 26. In the response to restriction requirement, received 18 April 2002, applicant reaffirmed the election of Group I, and further indicated that they elected the species of the nucleic acid set froth in SEQ ID NO:26. In view of such amendments to the claims and in view of applicant's election, claims 1 is fairly directed towards the elected invention and has been rejoined with the elected invention.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3, 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As presently worded, the invention of claims 3 and 8 read on full length SEQ ID NO: 26. Whether the fragment be the entire length or only a segment of SEQ ID NO: 26, the sequence represented by SEQ ID NO: 26 is but a fragment of an expressed sequence; see page 3, lines 4-5. The specification does not teach what the nucleotide sequence encodes nor does the specification teach in such full, clear and concise terms how this sequence could be used in a reproducible manner so as to enable its use.

7. While page 5 of the specification suggests that the nucleic acid sequences are "useful for the detection of an abnormality, such as a mutation, in the oligophrenin gene or in the transcripts of the oligophrenin gene," the specification is essentially silent as to what useful mutations are to be detected by use of SQ ID NO: 26.

8. Page 13, lines 20-22 of the specification state: "The ORF of the oligophrenin 1 gene as shown in SEQ ID n° 26 according to the invention encodes a protein of 802 amino acids with a relative molecular mass of 91 kD." A review of SEQ ID NO: 26 finds that consists of 3101 nucleotides. Since that it is a cDNA sequence, it stands to reason that the entire length encodes amino acid residues. Accordingly, the sequence of SEQ ID NO: 26 should encode 1,033 amino acids with 2 nucleotides left over. It is further noted that SEQ ID NO: 26 does not begin with a start sight, e.g., the codon "ATG." Interestingly, the amino acid sequence set forth on SEQ ID NO: 27 does depict an amino acid sequence of 802 amino acids (it would take 2,403 nucleotides to encode this sequence). However, the amino acid sequence of SEQ ID NO: 27 does not correspond to the nucleotide sequence of SEQ ID NO: 26. Accordingly, it is less than clear just what, if anything SEQ ID NO: 26 encodes and what fragments, assuming that there are some, would in fact be useful in some assay.

Response to argument

At page 3 of the response received 20 February 2003, applicant asserts:

> Contrary to the Examiners' position that SEQ ID NO:26 is "but a fragment of an expressed sequence" and that the specification "does not teach what the nucleotide sequence encodes . . . or how this sequence could be used in a reproducible manner", the present application teaches that SEQ ID NO:26 represents the cDNA fragment corresponding to the common open-reading frame (ORF) of the oligophrenin gene and encodes the protein of 802 amino acids at the coding region at nucleotides 639 to 3047 of SEQ ID NO:26. The skilled artisan can thus readily use this information in a reproducible

manner to obtain the claimed gene as well as to express the protein of SEQ ID NO:27 using the identified coding region in SEQ ID NO:26..

The above argument has been fully considered and has not been found persuasive. The record plainly states that the nucleic acid of SEQ ID NO:26 is a cDNA sequence. With a copy DNA (cDNA) sequence being the DNA copy of an mRNA transcript, the full length of the cDNA, sans a polyA tail, encodes an amino sequence. Accordingly, the entire length of the disclosed cDNA(SQ ID NO:26) is to encode a protein. It is noted that the cDNA represented by SEQ ID NO:26 does not contain a polyA tail, a feature common to cDNA reverse transcribed from mammalian mRNA. The absence of a polyA tail, when considering that the cDNA was derived from human, indicate that the cDNA is not complete. Additionally, attention is directed to page 3, penultimate paragraph, of the specification, which is reproduced below.

SEQ ID n° 26 represents the cDNA fragment corresponding to the common open-reading frame (ORF).

It is noted with particularity that applicant considered the cDNA to be but a "**fragment** corresponding to the common open-reading frame (ORF)" and not the complete cDNA sequence. (Emphasis added.)

9. In order for the cDNA to be useful for protein production, it must be in proper reading frame. The cDNA represented by SEQ ID NO:26 does not begin with a start site for transcription/translation, e.g., ATG. SEQ ID NO:26 begins with the nucleotide sequence "TGT," which codes for the amino acid threonine. Also, the length of SEQ ID NO:26 (3101 nucleotides) is not divisible by three, the number of nucleotides required for a codon, the basic unit of nucleotides that code for a given amino acid.

10. Applicant, in their response, directs attention to nucleotides 639 to 3047 of SEQ ID NO: 26 as encoding a polypeptide, and asserts that one of skill in the art would somehow be able to "use this information in a reproducible manner to obtain the claimed gene as well as to express the protein of SEQ ID NO:27 using the identified coding region in SEQ ID NO:26." It is noted, however, that applicant is claiming SEQ ID NO:26, not just nucleotides 639 to 3047 of SEQ ID NO:26. Additionally, the claims are not directed to a "gene." A gene is considered to comprise not only initiation and termination sequences, but also introns, promoter(s) and other regulatory sequences. None of these elements are present in the disclosed cDNA fragment. In any event, one would not be able to take full length SEQ ID NO:26 and express the alleged and deduced amino acid sequence corresponding to nucleotides 639 to 3047, and nucleotide 639 is not in proper reading frame with that of nucleotide 1 of said SEQ ID NO:26. Accordingly, one would not be able to use SEQ ID NO:26 to express the amino acid sequence allegedly encoded by this subsequence.

11. While applicant asserts that one would be able to reproducibly practice some method, the response fails to identify where the originally filed specification fully enables such method. Assuming *arguendo*, that one of skill could somehow use SEQ ID NO: 26 to express a protein, a position that the Office does not concede, the specification is essentially silent as to how the protein is to be used, or how one would ascertain that any such protein so produced would have its requisite activity. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200,

1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').

*****

"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

12. For the above reasons, and in the absence of convincing evidence to the contrary, the claims are rejected under 35 USC 112, first paragraph, as not being enabled by the disclosure.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 1, 3, 8 and 9 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

15. The specification discloses that SEQ ID NO: 26 encodes the common ORF for the gene oligophrenin 1 and that it encodes a polypeptide of 801 amino acids. A review of the specification finds that the length of SEQ ID NO: 26 does no correspond to a cDNA sequence that would encode a polypeptide of such length, that the sequence of nucleotides presented in SEQ ID NO: 26 do not encode such an amino acid sequence, and that no specific mutation or fragment(s) of SEQ ID NO: 26 have been found to be closely associated with any particular condition.

16. Claims 3, 8 and 9 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to argument

At page 4 of the response applicant states:

> By virtue of the present invention, the inventors have now identified and cloned the 'gene responsible for MRX, and this gene has been identified as the oligophrenin 1 gene which is the subject of the present claims. The nucleic acids of the invention are thus useful for the detection of an abnormality, such as a mutation, in the oligophrenin 1 gene, and such detection will be useful in permitting in vitro diagnosis and treatment of a neurological disorder associated with said abnormality. (Emphasis added.)

17. The above argument has been fully considered and has not been found persuasive. As an initial matter, it is noted with particularity that applicant has not cloned the complete gene. A gene is considered to be comprised or promoter sequences, introns, exons, etc. SEQ ID NO: 26,

however, is a fragmented cDNA sequence, which by default, must exclude promoter sequences and introns. Additionally, the cDNA represented by SEQ ID NO:26 is of such a reading frame that it would not encode the protein that applicant directs attention to and which is allegedly encoded by nucleotides 639 to 3047.

18. While applicant asserts that detection of he gene "will be useful," such futuristic desires and intimations do not satisfy the utility requirement as the invention must satisfy the utility requirement at the time of filing. It matters not whether the claim is drawn to a product or process; the claim must be drawn to an invention that satisfies the utility requirements as set forth under 35 USC 101 and as further developed in the Utility Guidelines. In support of this position, attention is directed to *Brenner, Comr. Pats. v. Manso*n, 148 USPQ 689 (US SupCt 1966):

> Whatever weight is attached to the value of encouraging disclosure and of inhibiting secrecy, we believe a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development, 22 without compensating benefit to the public. The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.
>
> * * *
>
> We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product. 24 That

> proposition seems to us little more than an attempt to evade the impact of the rules which concededly govern patentability of the product itself.
> This is not to say that we mean to disparage the importance of contributions to the fund of scientific information short of the invention of something "useful," or that we are blind to the prospect that what now seems without "use" may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.

19. Accordingly, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by GIBCO.

22. For convenience, claim 1, as amended, is reproduced below.

> 1. (Amended) Nucleic acid having a sequence selected from the group consisting of sequences SEQ ID n° 1 to SEQ ID n° 2526, and a homologous nucleic acid sequence thereof.

Page 4, penultimate paragraph defines the phrase "a homologous nucleic acid sequence thereof" thusly:

> "A homologous nucleotide sequence" is understood as meaning a sequence which differs from the sequences to which it refers by mutation, insertion, deletion or substitution of one or more bases.

Accordingly, claim 1 has been interpreted as encompassing nucleic acids that are considerably shorter than the original SEQ ID NO:26, including oligonucleotides.

23. GIBCO BRL Products & Reference Guide (GIBCO), page 17-19, discloses random primers. Said random primer composition is considered to have as an inherent property, at least one oligonucleotide that corresponds to "a homologous nucleic acid sequence" of SEQ ID NO: 26. Accordingly, GIBCO fairly teaches at least one embodiment of claim 1.

Conclusion

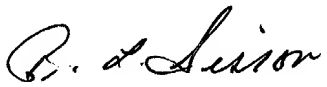
24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

25. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS